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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Timothy J. Barberich and James W. Young

Serial No.: 07/896,725 Group Art Unit: 1205

Filed: June 9, 1992 Examiner: L. Schenkman

Title: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-) ALBUTEROL

Record of Telephonic Interview

To: Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

This is not an amendment, nor it is intended to be responsive to any official Action from the Patent and Trademark Office. Rather it is intended to make of record the substance of a telephonic interview between Examiner Schenkman and applicants' undersigned representative on August 3, 1993.

On August 2, 1993 applicants' representative telephoned Examiner Schenkman and requested the opportunity to discuss the Examiner's final rejection of June 7, 1993 and applicant's response thereto submitted July 23, 1993. Examiner Schenkman graciously agreed to call applicant's representative after he had received and read the response.

On August 3, 1993, Examiner Schenkman called applicant's representative and indicated that he had received and read the response, and that it was his intention nonetheless to maintain his rejection. He indicated that the basis of his rejection was the belief that when there are two enantiomers, the person of skill always expects that one will be more active. Applicants

pointed out that in the present case the art was not silent on what the person of skill ought to expect. The art, described in earlier responses and declarations provided by applicants, teaches that there is no advantage to isolating either pure isomer over the racemate for the purpose of enhancing potency.

Examiner Schenkman then stated his belief that the art showed that the R-isomer would have fewer side effects. Applicants' representative explained that none of the art, available at the time of filing of the application, taught that there would be any advantage to using either isomer for diminution of side effects. In fact, the combined teachings of the art were clear on the point that there would be no advantage to using pure R-albuterol.

The Examiner asked what the declaration of Gunnar Aberg showed. Applicants' representative explained that the declaration showed that sensitization to spasmogens is associated with S-albuterol, but not with R, and that therefore there was a previously unappreciated advantage to the resolution and use of pure R-albuterol. The Examiner inquired whether that wasn't what Morley and Chapman had shown. Applicants' representative agreed that was indeed what Morley and Chapman had shown, but that both of the Morley and Chapman references appeared subsequent to the filing date of the instant application and were therefore independently supportive of applicants' position.

Examiner Schenkman reiterated his position that a person of skill would still expect one isomer to be better than the other. Had applicants isolated an unknown enantiomer or had the enantiomers been difficult to separate, and applicants devised a separation, he believed that might provide allowable subject matter, but under the present circumstances he felt R-albuterol would be unpatentable to applicants. Applicants' representative

pointed out that the pending claims were not to R-albuterol, per se, but to a use of R-albuterol and suggested a Jepson-type claim of the format:

> "In a method of using albuterol to treat asthma, the improvement which comprises reducing side effects by administering R-albuterol in place of racemic albuterol."

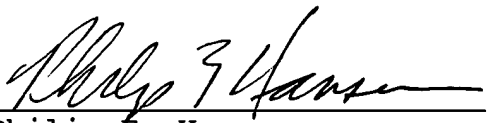
Examiner Schenkman did not believe that this would address his concerns either, because the treatment of asthma was a known use and the R-isomer was known isomer. He indicated that issue had been reached on this point, and the interview was then concluded.

On August 4, 1993 applicants' representative telephoned Examiner Schenkman to cite a 1987 decision of the Board of Patent Appeals and Interferences (ex parte Ferrari), which was believed highly relevant to the Examiner's concerns about the patentability of known enantiomers. Ferrari had sought claims to (-)-moprolol. Moprolol was known to exist as a racemic mixture of enantiomers, and the art would have led one to expect that the (-) enantiomer would possess essentially all of the known antihypertensive activity. The inventors found an unexpected beneficial result relating to cardiac side effects for the (-) enantiomer. The Board held that the claims were patentable on the basis of an unexpected, improved side effect profile. A copy of that decision is enclosed herewith for the convenience of the Examiner.

Also included for the convenience of the Examiner is a copy of an article by Spitzer et al. [New England Journal of Medicine 326, 501-506 (1992)] which emphasizes the clinical and therapeutic importance of the hypersensitivity reaction associated with racemic albuterol namely that it appears to lead

to increased risk of death from asthma or near fatal asthma (page 6, third and fourth paragraph and page 8, fourth and fifth full paragraphs). The use of optically pure R-albuterol, as claimed by applicants, avoids this serious side effect. However, such use of R-albuterol is neither taught nor suggested by the prior art.

Respectfully submitted,



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Dated: August 4, 1993

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